

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>109272.146</b>	<b>FOR FURTHER ACTION</b> <small>see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.</small>	
International application No. <b>PCT/US 00/ 28903</b>	International filing date (day/month/year) <b>18/10/2000</b>	(Earliest) Priority Date (day/month/year) <b>20/10/1999</b>
Applicant  <b>MICROBIA, INC.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.  
☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

**4. With regard to the title,**

- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established by this Authority to read as follows:

**5. With regard to the abstract,**

- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 2

- ☐ as suggested by the applicant. ☐ None of the figures.
- ☒ because the applicant failed to suggest a figure.
- ☐ because this figure better characterizes the invention.

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 00/28903

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 2-445 (complete); 1, 446-447 (partially)  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box 1.2

Claims Nos.: 2-445 (complete); 1, 446-447 (partially)

In view of the large number of claims present on file as well as their wording, the International Search Agency considers that it is difficult, if not impossible, to determine the matter for which protection is actually sought and that the present application fails to comply with the clarity and conciseness requirements of Article 6 PCT (see also Rule 6.1(a) PCT) to such an extent that a meaningful search is impossible.

Moreover, the claims relate to methods defined only by reference to a desirable characteristic, namely "... modulating the expression of a gene involved in regulation of secondary metabolite production in a manner..." that (i) improves the yield of the secondary metabolite (claims 1-64), (ii) improves the productivity of the secondary metabolite (claims 65-127), (iii) increases the flux or excretion of the secondary metabolite, (claims 128-190), (iv) decreases the production of side products or competing secondary metabolites (claims 191-253), (v) alters the characteristics of the fungus (claims 254-319), (vi) causes conditional lysis (claims 320-382) and (vii) increases resistance to the deleterious effects of exposure to a secondary metabolite (claims 383-445) as well as to related products (genetically modified fungi, claim 446) and uses thereof (method of making a secondary metabolite, claim 447). The claims cover all methods having this characteristic, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such methods. In the present case, the claims so lack support and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the methods by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Furthermore, according to Rule 13 PCT an application must relate to one invention only or to a group of inventions so linked as to form a single general inventive concept, i.e. having at least one common technical feature defining a contribution over the known prior art. In the present case, the common technical feature among the different groups of inventions seems to be "...the modulation of the expression of a gene involved in the regulation of secondary metabolite production ... for improving the production of a secondary metabolite by a fungus ...". However, this concept was already known in the prior art (see disclaimers in claim 1, bibliographic references in the description of the application as well as the partial ISR). Therefore, in principle seven different groups of inventions could be identified corresponding to the seven independent claims of the present application, namely methods for improving the production of a secondary metabolite modulating the expression of a gene involved in the regulation of secondary metabolite production in a manner that : (i) improves the yield of the secondary metabolite (claims 1-64), (ii) improves the productivity of the secondary metabolite (claims 65-127), (iii) increases efflux or excretion of the

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

secondary metabolite (claims 128-190), (iv) decreases the production of side products or competing secondary metabolites (claims 191-253), (v) alters the characteristics of the fungus (claims 254-319), (vi) causes conditional lysis (claims 320-382), (vii) increases resistance to the deleterious effects of exposure to a secondary metabolite (claims 383-445) as well as related genetically modified fungi and uses thereof for each group (claims 446-447, partially). However, in view of the references cited in the application and in the partial ISR, the ISA fails to see which is the single inventive concept among the different embodiments corresponding to the dependent claims of each group of inventions. Thus, each and every group identified above comprises several subgroups of inventions, such as : (i) type of modulation and/or modulator, (ii) type and effects of the genes involved in the regulation of the secondary metabolite production, (iii) type of secondary metabolite, etc...

In conclusion, the claims do not fulfil the requirements of Articles 5 and 6 PCT and Rule 13 PCT. A meaningful search over the whole of the claimed scope is impossible and consequently, the search has been carried out only for those parts of the application which do appear to be (i) clear, concise, technically supported and (ii) which correspond to the first group of invention (claims 1 and 446-447, partially), namely those parts relating to methods for increasing the yield of a secondary metabolite using the "fungal regulators" of Table 1 (examples 3-5). However, in view of the document W099/25735 no common inventive concept seems to be present among these several fungal regulators.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

National Application No  
PCT/US 00/28903

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 C07K14/37 C12N15/80 C12P21/00 C12R1/645

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 C07K C12N C12P C12R

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 25735 A (MICROBIA INC) 27 May 1999 (1999-05-27) the whole document ---	1,446, 447
X	WO 99 25865 A (MICROBIA INC) 27 May 1999 (1999-05-27) the whole document ---	1,446, 447
X	EP 0 357 119 A (GIST BROCADES NV) 7 March 1990 (1990-03-07) the whole document, in particular page 8 line 52 to page 9 lines 3 ---	1,446, 447
X	US 5 665 543 A (LEICHTFRIED FRANZ ET AL) 9 September 1997 (1997-09-09) the whole document, in particular columns 31-34 --- -/--	1,446, 447

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

13 March 2001

Date of mailing of the international search report

04.04.01

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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 00/28903

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 00 37629 A (WISCONSIN ALUMNI RES FOUND) 29 June 2000 (2000-06-29) cited in the application the whole document -----	1,446, 447

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/28903

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9925735	A	27-05-1999	AU 1529099 A AU 1797999 A EP 1049797 A EP 1032590 A WO 9925865 A	07-06-1999 07-06-1999 08-11-2000 06-09-2000 27-05-1999
WO 9925865	A	27-05-1999	AU 1529099 A AU 1797999 A EP 1049797 A EP 1032590 A WO 9925735 A	07-06-1999 07-06-1999 08-11-2000 06-09-2000 27-05-1999
EP 0357119	A	07-03-1990	AT 130033 T AU 631371 B AU 3956889 A AU 631806 B AU 3956989 A DE 68924745 D DK 393089 A DK 393189 A EP 0354624 A ES 2081831 T FI 893722 A FI 893723 A GR 3018782 T HU 51335 A,B IE 72167 B JP 2167078 A JP 2954601 B JP 2150284 A JP 3095391 B JP 2000342289 A PT 91410 A,B PT 91411 A,B US 5462862 A US 5747285 A US 5108918 A	15-11-1995 26-11-1992 15-02-1990 10-12-1992 15-02-1990 14-12-1995 12-02-1990 12-02-1990 14-02-1990 16-03-1996 12-02-1990 12-02-1990 30-04-1996 28-04-1990 26-03-1997 27-06-1990 27-09-1999 08-06-1990 03-10-2000 12-12-2000 08-03-1990 08-03-1990 31-10-1995 05-05-1998 28-04-1992
US 5665543	A	09-09-1997	US 5976793 A US 6136779 A US 5863733 A US 6203976 B US 6165712 A US 5846720 A US 5580722 A AU 660405 B AU 6140090 A CA 2063822 A EP 0483249 A JP 4506902 T WO 9101379 A	02-11-1999 24-10-2000 26-01-1999 20-03-2001 26-12-2000 08-12-1998 03-12-1996 29-06-1995 22-02-1991 19-01-1991 06-05-1992 03-12-1992 07-02-1991
WO 0037629	A	29-06-2000	AU 2180100 A	12-07-2000

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STARTZEIT	04-APR-01 15:46
TELEFONNUMMER	00016175265000
NAME (KENNUNG)	617 526 5000
ÜBERTR.-MODUS	EMMR
AUFLÖSUNG	STD
ÜBERTR. SEITEN	010
MAILBOX	AUS
GESICHERT	AUS
INFORMATIONSCODE	OK
WAHLWIEDERHOLUNG	00
DAUER	04'46
JOB-NUMMER	119

DIESE ÜBERTRAGUNG IST VOLLSTÄNDIG.

LETZTE ERFOLGR. SEITE 010